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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,827	03/10/2004	Linda M. Weigel	6395-68161-01	5019

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KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET
SUITE 1600
PORTLAND, OR 97204

EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
10/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,827	WEIGEL ET AL.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2007 and 27 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-50* is/are pending in the application.

4a) Of the above claim(s) *32-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30,31 and 39-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *6/2007*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of SEQ ID NO: 25 in the reply filed on June 5, 2007 is acknowledged. The traversal is on the ground(s) that "it is not an undue burden on the Examiner to each the claimed polynucleotide sequences together. With regard to the remarks in the Office action: the Office action acknowledges that SEQ ID NO: 9, SEQ ID NO: 12, SEQ ID NO: 14 and SEQ ID NO: 16 all encode a polypeptide of identical amino acid sequence. However, the Office action alleges that since then polynucleotide sequences are different ('apples') even though the encoded polypeptides is the same (a single 'orange') they simply can't be examined together. The Office action alleges this is because the polynucleotides were isolated from different species of bacteria which have different biological properties (see page 4). Applicants do not deny that different species of bacteria have different biological properties. However, the presently claimed methods are used to detect a specific polynucleotide that encodes a protein with a defined function. All of the biological properties of the detected bacteria are not at issue. The claimed methods are performed using probes (which can be synthetically produced) that bind a specified nucleic acid sequence. Applicants do not deny that MPEP states that 'nucleotide sequences encoding different proteins are ....deemed to be normally constitute independent and distinct inventions' (see the Office action at page 4). However, with regard to at least SEQ ID NO: 9, SEQ ID NO: 12, SEQ ID NO: 14 and SEQ ID NO: 16 this is simply NOT the situation in the present case. The polynucleotides set forth as SEQ ID NO: 9, SEQ ID NO: 12, SEQ ID NO: 14 and SEQ ID NO: 16 all encode exactly the SAME protein. As noted in the prior response, and as acknowledged in the Office action (see page 4), the MPEP § 2434 states: '[n]ucleotide

sequences encoding the same protein are not considered to be independent and distinct and will continue to be examined together.' Thus, it is clear that SEQ ID NO: 9 should be examined with at least SEQ ID NO: 12, SEQ ID NO: 14 and SEQ ID NO: 16. In addition, as the QRDR proteins encoded by SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 13 and SEQ ID NO: 15 differ from the polypeptide encoded by SEQ ID NO: 9 by at most two amino acids, and all of these nucleic acid sequence encode proteins with the same function. Thus, Applicants submit that all of SEQ ID NOs: 9-14 should be examined a single application. It would not represent a burden on the Patent Office to examine the closely related sequences in a single patent application".

The above arguments have been fully considered and have not been found persuasive toward the withdrawal of the lack unity requirement nor persuasive toward the relaxation of same such that SEQ ID NO: 9-16 will be examined together. First, although SEQ ID NO: 9, SEQ ID NO: 12, SEQ ID NO: 14 and SEQ ID NO: 16 all encode a polypeptide of identical amino acid sequence, since SEQ ID NO: 9, SEQ ID NO: 12, SEQ ID NO: 14 and SEQ ID NO: 16 are quinolone resistance determining region (QRDR) sequences from the gyrA genes of *Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae,* and *Serratia marcescens* which have different nucleotide sequences and are from different gyrA genes, and SEQ ID Nos: 9, 12, 14, and 16 are not polypeptide sequences but are nucleotide sequences (see the specification, Figures 1A, 1B, 2, and 3), SEQ ID Nos: 9, 12, 14, 16 are patentably distinct sequences. Furthermore, since SEQ ID Nos: 9-16 are from the gyrA genes of *Escherichia coli, Citrobacter freundii, Enterobacter aerogenes, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Providencia stuartii, and Serratia marcescens* which encode different gyrAs, SEQ

ID Nos: 9-16 are patentably distinct sequences. Second, although applicant argues that "it is clear that SEQ ID NO: 9 should be examined with at least SEQ ID NO: 12, SEQ ID NO: 14 and SEQ ID NO: 16. In addition, as the QRDR proteins encoded by SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 13 and SEQ ID NO: 15 differ from the polypeptide encoded by SEQ ID NO: 9 by at most two amino acids, and all of these nucleic acid sequence encode proteins with the same function", since the claims are directed to a method related to nucleic acids and are not directed to a method related to polypeptides, applicant appears to compare an apple (ie., polypeptide) to an orange (ie., nucleic acid). Third, MPEP 2434 states that "[N]ucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121". Since SEQ ID NOs: 9-16 are from different gyrase A genes of *Escherichia coli*, *Citrobacter freundii, Enterobacter aerogenes, Enterobacter cloacae, Klebsiella oxytoca, Klebsiella pneumoniae, Providencia stuartii,* and *Serratia marcescens* and SEQ ID NOs: 9-16 are not from a single gene, according to MPEP 2434, SEQ ID Nos:9-16 are patentably distinct sequences and should be restricted to different groups. Fourth, although MPEP 2434 states that "the Commissioner has partially waived the requirements of 37 CFR 1.141 and will permit a reasonable number of such nucleotide sequences to be claimed in a single application. Under this policy, in most cases, up to 10 independent and distinct nucleotide sequences will be examined in a single application without restriction", MPEP 2434 does not require that the examiner must examine 10 independent and distinct nucleotide sequences together as argued by applicant. Based on above reasons, the requirement is still deemed proper and is made FINAL. Since there are two claims 44 and 45 in the amendments filed on June 27,

2007, claims 30-48 are renumbered as claims 30-50. In view of elections on February 7, 2007 and June 5, 2007, claims 30, 31, and 39-50 will be examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Enablement

Claims 30, 31, and 39-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that quinolone susceptibility of the *Escherichia coli* in a sample can be determined using the methods recited in

claims 30, 31, and 39-50 by combining the sample with a nucleic acid probe wherein the probe selectively hybridizes to a nucleic acid sequence set forth as SEQ ID NO:9 or a complementary sequence thereof. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether quinolone susceptibility of the *Escherichia coli* in a sample can be determined using the methods recited in claims 30, 31, and 39-50 by combining the sample with a nucleic acid probe wherein the probe selectively hybridizes to a nucleic acid sequence set forth as SEQ ID NO:9 or a complementary sequence thereof.

Claims 30, 31, and 39-50 are directed to a method of determining the quinolone resistance of *Escherichia coli* by combining the sample with a nucleic acid probe wherein the probe selectively hybridizes to a nucleic acid sequence set forth as SEQ ID NO:9 or a complementary sequence thereof. Since claims 30, 31, 39, 42-44, 49, and 50 does not limit the size of the probe and claims 40, 41, and 45-47 requires that the size of the probe is 10-50 nucleotides, SEQ ID NO: 25 recited in claim 41 which is elected by applicant is a nucleic acid probe recited in claims 30, 31, and 39-50. Since the results from sequence alignments show that SEQ ID No: 25 can 100% hybridize with a nucleic acid from bacterium *Shigella flexneri* 2a and can 100% hybridize with gyr A gene from *Shigella sonnei* (see attached sequence alignments), the nucleic acid probe recited in claims 30, 31, and 39-50 is a non-specific nucleic acid probe and can hybridize with a nucleic acid in other bacteria strains which are not *Escherichia coli*. Therefore, it is unclear how the presence of the hybridization between the nucleic acid probe recited in claims 30, 31, and 39-50 and a nucleic acid in the sample can indicate quinolone susceptibility of the *Escherichia coli* in the sample.

For the reasons discussed above, it would have required undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention claimed. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the working examples provided and scarcity of guidance in the specification, and the unpredictable nature of the art. The undue experimentation at least includes to test whether quinolone susceptibility of the *Escherichia coli* in a sample can be determined using the methods recited in claims 30, 31, and 39-50 by combining the sample with a nucleic acid probe wherein the probe selectively hybridizes to a nucleic acid sequence set forth as SEQ ID NO:9 or a complementary sequence thereof.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 30, 31, and 39-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 30 is rejected as vague and indefinite in view of the phrase "SEQ ID NOs: 9-16" because SEQ ID NOs: 10-16 have not been elected. Furthermore, it is unclear that "a nucleic acid" in line 7 means a nucleic acid probe or means a nucleic acid sequence comprising SEQ ID NO:9. Please clarify.

7. Claim 39 is rejected as vague and indefinite in view of the phrase "SEQ ID NOs: 1-9" because SEQ ID NOs: 1-8 have not been elected. Please clarify.

8. Claim 41 is rejected as vague and indefinite in view of the phrase "SEQ ID NOs: 25-33" because SEQ ID NOs: 26-33 have not been elected. Please clarify.

9. Claims 42-44 are rejected as vague and indefinite because SEQ ID NO: 9 only has nucleotides 1-120 and does not have nucleotides 121 to 613 recited in claim 42, nucleotides 199 to 318 recited in claim 42, and nucleotides 239 to 663 recited in claim 44. Please clarify.

10. Claim 46 is rejected as vague and indefinite because, from the claim, it is unclear how to use a polymerase chain reaction (PCR), ligase chain reaction, or a nucleotide array for determining the quinolone resistance of an *Enterobacteriaceae species*. Please clarify.

Conclusion

11. No claim is allowed.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu,. Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

October 15, 2007

FRANK LU
PRIMARY EXAMINER